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Robot-assisted Radical Prostatectomy: Ready To Be Counted?

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In the current issue of *European Urology*, Tewari et al. [1] present a remarkable systematic review examining perioperative outcomes and margin rates of open radical prostatectomy (ORP), laparoscopic radical prostatectomy (LRP), and robot-assisted radical prostatectomy (RARP). They found that the rate of adverse events was lower with RARP than with ORP or LRP. This is the latest in a growing body of publications that critically examine the comparative effectiveness of different approaches to radical prostatectomy (RP) [2–5].

Since the early proof-of-principle studies in Europe [6,7] and the establishment of the approach as a viable, reproducible surgical tool in the United States [8], robotic surgery has transformed the discipline of urology, and nowhere has its effect been felt more than in the technique of RP. In 2001, <200 of the roughly 70 000 patients undergoing RP in the United States underwent RARP. By 2008, nearly two-thirds of patients chose the robot-assisted option [2]. The rapidity of this expansion has rivaled that of the Internet and has far exceeded that of laparoscopic nephrectomy, cell phones, or the personal computer [9].

The expansion of this technology did not happen in a controlled, scientific, scholarly manner. The initial adopters of the procedure came from places such as Detroit, Michigan; San Ramon, California; and Birmingham, Alabama (among others). In a gothic interpretation, the expansion of RARP has been attributed to the marketing genius of a monopolistic manufacturer endorsed by overenthusiastic surgeons anxious to secure a competitive advantage [10]. There is some truth to this observation: Surgeons and hospitals have increasingly created Web sites, and the information presented there is often uncontrolled, unedited, and unproven [11]. However, patients are undeniably voting with their feet, and robotic surgery

centers of excellence have sprung up in response to patient demand [12].

How do we measure the real benefits of this new technology? In theory, the best way is through a structured review of randomized clinical trials involving multiple institutions, well-defined patient demographics, structured follow-up, and predetermined outcome measurements. Such a review would provide the highest level of scientific evidence [13]. However, such trials are difficult to perform. Indeed, in a procedure in which the surgeon is an independent variable in determining outcomes, there is a hint that structured reviews of cohort studies might yield more generalizable conclusions than would results from narrowly focused randomized trials. Several authors have attempted to perform such structured reviews. In a widely cited study, Ficarra et al. [5] reviewed studies that internally compared RARP, LRP, and ORP. The study concluded that while RARP was associated with decreased blood loss, there were no differences in the rates of complications or positive margins. However, as suggested by Tewari et al, meta-analyses based on comparative articles, although informative, do not represent most of the literature available in this area, which are single-cohort studies. Thus, while >10 000 records were reviewed by Ficarra and colleagues, only 37 met the criteria for inclusion in the systematic review.

In a landmark article, Hu and colleagues [3] determined the comparative effectiveness of ORP and minimally invasive RP (MIRP). Using administrative data from the Surveillance Epidemiology and End Results (SEER)–Medicare database, they studied complication rates and functional outcomes in men undergoing RP from 2003 to 2007. This database links cancer registries covering 26% of the US population (SEER) with administrative data on Medicare patients >65 yr old. Since administrative claims prior to October 2008 did not distinguish between RARP and

LRP, both techniques were incorporated in a single term (MIRP). MIRP was associated with a shorter hospital stay and a lower transfusion rate, but not with a lower overall complication rate. In a follow-up study, the Hu group [4] analyzed outcomes of RP in the entire Medicare population between 2003 and 2007. In this analysis, they confirmed the superiority of MIRP for length of hospitalization and transfusions but also demonstrated a clear decrease in overall or system-specific complications with MIRP.

How does the Tewari paper fit into this setting? There are important differences in methodology between this study and the previous ones. First, the authors were able to distinguish between LRP and RARP. Second, the study did not restrict its analysis to comparative studies. Finally, the study was not confined to the Medicare population, or indeed to just patients from the United States.

Tewari et al. used the criteria defined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement [14] to select >5000 full-text manuscripts that were published in the English language between 2002 and 2010. They then excluded manuscripts that may have had duplicate populations, series prior to 1990, and series that may have reflected the learning curve of the surgeons, which left 400 publications that met the criteria for analysis. To account for inherent differences in demographic and tumor characteristics among studies, the authors performed propensity-score adjustment for multiple patient, surgeon, and hospital factors [15]. While such a statistical technique is an imperfect substitute for randomization, it provides higher-quality evidence than single-surgeon cohort studies. Tewari et al. concluded that robotic assistance was associated with more favorable perioperative outcomes, including decreased rates of blood transfusions, fewer intraoperative and postoperative complications, and shorter length of stay. This finding was similar to the conclusions in the recent Kowalczyk et al. paper [4]. Importantly, Tewari et al. showed that positive surgical margin rates were similar for open and robotic surgery.

It is important to remember that meta-analyses report on “averages.” It is commendable that Tewari and colleagues used funnel plots as visual aids to exclude the possibility of systematic heterogeneity (difference in effect size between smaller and larger studies) or publication bias. The shape of a funnel plot can vary quite dramatically, depending on what measure is used for the y-axis. Tewari et al. used sample size for the y-axis, and it appears that some of the funnel plots are not perfectly symmetrical. This observation suggests that some of the differences may be related to publication bias or the effect of sample size. Notwithstanding, this publication strongly suggests that across the board, there are fewer complications following RARP than ORP or LRP.

It is possible that the better outcomes reported following RARP reflect an extensive regionalization of prostate cancer surgical care to high-volume providers rather than any inherent benefit from robotic technology. In the United States, the introduction of robotics resulted in 35% of hospitals that owned a robot performing 85% of all cases, with 9% of hospitals performing 57% of all cases [16]. Indeed,

there is substantial evidence to support the idea that “practice does make perfect” and, therefore, that prostatectomy outcomes are better when performed by high-volume surgeons [17]. Indeed, it is important to note that RARP is not invariably better than ORP; an inexperienced surgeon performing a robot-assisted procedure would be expected to achieve poorer results than an experienced surgeon performing an open procedure. After all, average tennis players are better when they use a titanium-framed racket, but Martina Navratilova, wooden racket or not, will still beat most players any day of the week and twice on Sunday!

Albert Einstein is credited with saying, “Not everything that can be counted counts, and not everything that counts can be counted.” Many nuances of robotic surgery cannot be counted, but Tewari and colleagues have done an extraordinary job of counting what can be counted.

Conflicts of interest: The authors have nothing to disclose.

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Walking the Tightrope: Balancing Cancer Control, Urinary Continence, and Sexual Function—A Programmatic Evolution

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Thanks for the opportunity to respond to the editorial comments presented by Trinh et al. [1]. We appreciate the thoughts on the methodology of meta-analysis. This methodology is robust and gives us a good idea about outcomes in terms of margin rates and perioperative complications. While Trinh et al. correctly point out that our paper demonstrates that margin rates are comparable between open and robotic assisted radical prostatectomy (RARP), our paper also demonstrates that the laparoscopic approach results in an increased risk for positive margins when compared to RARP. It also shows that in terms of perioperative complications, RARP is the safest among these approaches [2].

One thing that is difficult to show using a meta-analytic approach is the impact of innovations and refinements that have occurred in robotic surgery since its inception. In addition to achieving negative margins and reduced surgical complications, RARP seeks to achieve the postoperative goals of continence and return of sexual function. It is in the pursuit of these *trifecta goals* for prostatectomy that RARP can have

the greatest impact. For example, in our own surgical cohort, we have been able to bring incremental improvements to the procedure over the years to achieve negative margin rates, urinary continence, and return of sexual function in patients who had good baseline sexual function (International Index of Erectile Function >21) and were candidates for good nerve sparing (grade 1) [2] in ranges >90% in all domains. By relating these trends with our published literature, it can be seen that these innovations have affected outcomes and reflect the process of learning a complex procedure such as radical prostatectomy (Fig. 1 [3–13]).

Initially, we worked on detailed trizonal neural architecture and adopted an athermal technique for nerve sparing [10]. Later on, the development of techniques such as total reconstruction of the vesico-urethral junction has proven to be a safe and effective way to achieve an early return of continence with significant gains when compared to the previous gold standard of no or partial reconstruction [3]. The incorporation of visual cues in surgery has yielded improvements in negative margins, allowing experienced surgeons to make informed intraoperative oncologic decisions [9]. Through adopting a risk-stratified approach to nerve-sparing RARP, we have been able to balance the risk of positive margins with preserving urinary and sexual function, achieving the successful outcomes seen today [4,8]. With these progressive innovations, RARP has seen greater success in achieving optimal outcomes in all areas of the trifecta goals—negative margins, urinary continence, and return to sexual function—as more and more patients are being treated at our surgical center.

Similar developments and refinements are occurring at other programs [14–16]. It would be great to pool the data for similar incremental improvements from multiple institutions and look across the board at the field of innovations in an effort to determine their relationship with improved trifecta outcomes. This is a challenge to tackle in future reviews.